IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

In re Application of:

Christopher J. M. MEADE et al. Examiner: P. Spivack

Serial No.: 10/614,362 Group Art Unit: 1614

Filed: July 7, 2003 Confirmation No.: 7889

Title: NEW PHARMACEUTICAL COMPOSITIONS BASED ON NEW ANTICHOLINERGICS AND NK_1 RECEPTOR ANTAGONISTS

REQUEST FOR REFUND

Mail Stop 16
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Further to applicants filing of March 28, 2008 in the above-identified application (a copy of which is attached hereto), Applicants hereby request a refund in the amount of $460.00. Applicant inadvertently paid fees for a two-month extension of time ($460.00) instead of a one-month extension of time ($120.00). Therefore, it is respectfully requested that the amount for a two-month extension of time, i.e., $460.00, be refunded to counsel's Deposit Account No. 13-3402.

Respectfully submitted,

/John A. Sopp/

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Attorney/Agent for Applicants

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Attorney Docket No.: BIC-1363

Filed: April 11, 2008

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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) 1/1363

In re Application of Christopher J. M. MEADE et al.	
Application Number 10/614,362	Filed July 7, 2003
For NEW PHARMACEUTICAL COMPOSITIONS BASED ON NEW ANTICHOLINERGICS AND NK$_1$ RECEPTOR ANTAGONISTS	
Group Art Unit 1614	Examiner P. Spivack

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a response in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- ☒ One month (37 CFR 1.17(a)(1)) $120.00
- ☐ Two months (37 CFR 1.17(a)(2)) $_____
- ☐ Three months (37 CFR 1.17(a)(3)) $_____
- ☐ Four months (37 CFR 1.17(a)(4)) $_____
- ☐ Five months (37 CFR 1.17(a)(5)) $_____

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ _____.

☒ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 13-3402.

I have enclosed a duplicate copy of this sheet.

I am the ☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71

Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☒ attorney or agent of record.

☐ attorney or agent under 37 CFR 1.34(a).

Registration number if acting under 37 CFR 1.34(a). _____.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

March 28, 2008
Date

/John A. Sopp/
Signature

John A. Sopp, Reg. No. 33,103
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

Burden Hour Statement: This form is estimated to take 0.1 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Christopher J. M. MEADE et al. Examiner: P. Spivack

Serial No.: 10/614,362 Group Art Unit: 1614

Filed: July 7, 2003 Confirmation No.: 7889

Title: NEW PHARMACEUTICAL COMPOSITIONS BASED ON NEW ANTICHOLINERGICS AND NK_1 RECEPTOR ANTAGONISTS

REPLY AFTER FINAL REJECTION

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Final Office Action mailed November 28, 2007, kindly amend the above-identified application as follows. A request for a one-month extension of time is filed herewith.

Amendments and additions to the **Claims** are reflected in the listing of claims, which begins on page 2 of this paper.

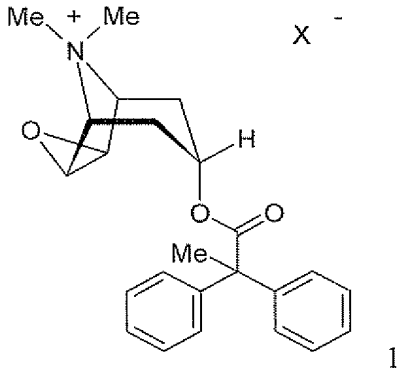
Remarks/Arguments begin on page 11 of this paper.

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Previously presented) A pharmaceutical composition for the treatment of chronic obstructive pulmonary disease comprising:

(a) one or more anticholinergics of formula 1



1

wherein:

X- is an anion with a single negative charge,

or an enantiomer, mixture of enantiomers, racemate, solvate, or hydrate thereof; and

(b) one or more NK_1 receptor antagonists,

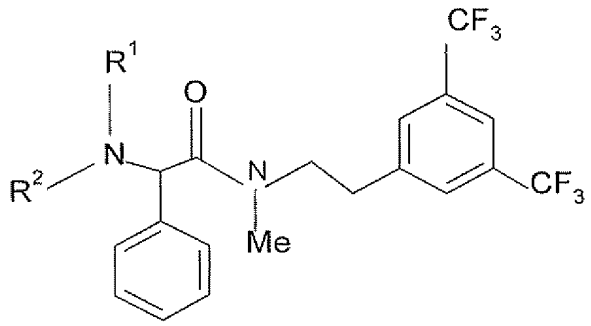
or an enantiomer, mixture of enantiomers, racemate, solvate, or hydrate thereof.

2. (Previously Presented) The pharmaceutical composition according to claim 1, wherein X^- is chloride, bromide, iodide, sulphate, phosphate, nitrate, maleate, acetate, citrate, fumarate, tartrate, oxalate, succinate, benzoate, 4-toluenesulphonate, or methanesulphonate.

3. (Previously Presented) The pharmaceutical composition according to claim 1, wherein X^- is bromide.

4. (Currently Amended) The pharmaceutical composition according to claim 1, wherein the NK_1 receptor antagonists are selected from among (*S*)-*N*-[2-[3,5-bis(trifluoromethyl) phenyl]ethyl]-4-(cyclopropylmethyl)-*N*-methyl-α-phenyl-1-piperazineacetamide (+)-(2S, 3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-

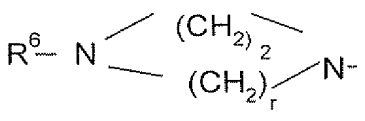
phenylpiperidine, (4R)-4-hydroxy-1-[(1-methyl-1H-indol-3-yl)carbonyl]-L-pyrolyl-N-methyl-3-(2-naphthalenyl)-N-(phenylmethyl)-L-alaninamide, (2R,4S)-N-[1-{3,5-bis(trifluormethyl)-benzoyl}-2-(4-chlorobenzyl)-4-piperidinyl]-quinoline-4-carboxamide, (S)-1-[2-[3-(3,4-dichlorphenyl)-1(3-isopropoxyphenylacetyl)piperidin-3-yl]ethyl]-4-phenyl-1-azaniabicyclo [2.2.2]octane, (R)-1[N-(2-methoxybenzyl)acetylamino]-3-(1H-indol-3-yl)-2-[N-(2-(4-(piperidinyl)piperidin-1-yl)acetyl)amino]propane, (S)-(-)-N(alpha-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide, 1-(3-(3,4-dichlorophenyl)-1-(3,4,5-trimethoxybenzoyl)-3-pyrrolidinyl)-4-phenyl-piperidin-morpholinecarboxamide, 2-(2-naphthyl)-1-N-[(1R, 2S)-2-N-[2(H)indol-3-ylcarbonyl]aminocyclohexanecarbonyl]-1-[N'-ethyl-N'-(4-methylphenylacetyl)]diaminoethane, (1R,2S)-2-N[1(H)indol-3-yl-carbonyl]1-N-{Nα(p-tolylacetyl)-N-D-3-(2-naphthyl)alanyl}diaminocyclohexane, (R)-3(1-[2-(4-benzoyl-2-(3,4-difluorophenyl)-morpholin-2-yl)ethyl]-4-phenylpiperidin-4-yl)-1-dimethylurea, N-[2(S)-(3,4-dichlorophenyl)-4-[4-(2-oxoperhydropyrimidin-1-yl)piperidin-1-yl]butyl]-N-methylbenzamide dihydrochloride, ~~Neuronorm,~~ N-(2-(3,4-dichlorophenyl)-4-(spiro(isobenzofuran-1(3H),4'-piperidin)-1'-yl)butyl)-N-methylbenzamide, 2-(R)-(1-(R)-3,5-bis(trifluoromethyl)phenylethoxy)-3-(S)-(4-fluoro)phenyl-4-(3-oxo-1,2,4-triazol-5-yl)methylmorpholine, (2S,3S-*cis*)-2-diphenylmethyl)-N-1-azabicyclo-[2.2.2]octan-3-amine, [3-[[2-[1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3(S)-(4-fluorophenyl)-morpholin-4-yl]methyl]-4,5-dihydro-5-oxo-1H-1,2,4-triazole-1-phosphonic acid bis(N-methyl-D-glucamine) salt, (aR,9R)-7-[3,5-bis(trifluoromethyl)benzyl]-8,9,10,11-tetrahydro-9-methyl-5-(4-methylphenyl)-7H-[1,4]diazocino[2,1-g][1,7]naphthyridine-6,13-dione, (2S,3S)-N-[2-methoxy-5-[5-(trifluoromethyl)-1-tetrazolyl]benzyl]-N-(2-phenylpiperidin-3-yl)amine dihydrochloride, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-{4-[(3-hydroxy-propyl)-methyl-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-[4-(2-hydroxy-1-hydroxymethyl-ethylamino)-piperidin-1-yl]-N-methyl-2-phenylacetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-[4-(cyclopropylmethyl-methyl-amino)-piperidin-1-yl]-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2--{4-[(2-hydroxy-ethyl)-(3-hydroxy-propyl)-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-{4-[cyclopropylmethyl-(3-hydroxy-propyl)-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, or an arylglycinamide compound of formula 3



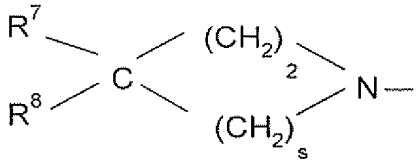
3

wherein:

R^1 and R^2 together with the N to which they are bound form a ring of formula



and



wherein r and s are each 2 or 3;

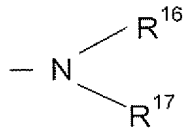
R^6 is H, -C_1-C_5-alkyl, C_3-C_5-alkenyl, propynyl, hydroxy(C_2-C_4)alkyl, methoxy(C_2-C_4)alkyl, di(C_1-C_3)alkylamino(C_2-C_4)alkyl, amino(C_2-C_4)alkyl, amino, di(C_1-C_3)alkylamino, monofluoro- to perfluoro(C_1-C_2)alkyl, N-methylpiperidinyl, pyridyl, pyrimidinyl, pyrazinyl or pyridazinyl,

R^7 is one of (a) to (d),

(a) hydroxy

(b) 4-piperidinopiperidyl,

(c)



wherein R^{16} and R^{17} are each independently H, (C_1-C_4)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_2-C_4)alkyl, dihydroxy(C_2-C_4)alkyl, (C_1-C_3)alkoxy(C_2-C_4)alkyl, phenyl(C_1-C_4)alkyl or di(C_1-C_3)alkylamino(C_2-C_4)alkyl, and

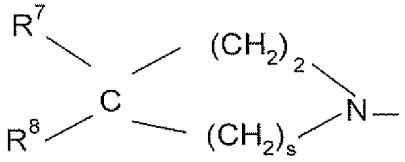
R^8 is H,

or an enantiomer, mixture of enantiomers, or racemate thereof.

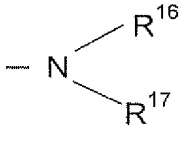
5. (Previously presented) The pharmaceutical composition according to claim 1, wherein the NK_1 receptor antagonists are selected from the group consisting of (*S*)-*N*-[2-[3,5-bis(trifluoromethyl) phenyl]ethyl]-4-(cyclopropylmethyl)-*N*-methyl-α-phenyl-1-piperazineacetamide, (+)-(2S, 3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine, (2S,3S-*cis*)-2-diphenylmethyl)-N-1-azabicyclo-[2.2.2]octan-3-amine, (2S,3S)-N-[2-methoxy-5-[5-(trifluoromethyl)-1-tetrazolyl]benzyl]-N-(2-phenylpiperidin-3-yl)amine dihydrochloride, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-{4-[(3-hydroxy-propyl)-methyl-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-[4-(2-hydroxy-1-hydroxymethyl-ethylamino)-piperidin-1-yl]-N-methyl-2-phenylacetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-[4-(cyclopropylmethyl-methyl-amino)-piperidin-1-yl]-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-{4-[(2-hydroxy-ethyl)-(3-hydroxy-propyl)-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-{4-[cyclopropylmethyl-(3-hydroxy-propyl)-amino]-piperidin-1-yl}-N-methyl-2-phenyl-acetamide, or an arylglycinamide compound of formula 3

wherein:

R^1 and R^2 together with the N to which they are bound form a ring of formula



wherein s is 2 or 3;

R^7 is 

,

wherein R^{16} and R^{17} are each independently H, $(C_1$-$C_4)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_2$-$C_4)$alkyl, dihydroxy$(C_2$-$C_4)$alkyl, $(C_1$-$C_3)$alkoxy$(C_2$-$C_4)$alkyl, phenyl$(C_1$-$C_4)$alkyl or di$(C_1$-$C_3)$alkylamino$(C_2$-$C_4)$alkyl, and

R^8 is H,

or an enantiomer, mixture of enantiomers, or racemate thereof.

6. (Previously Presented) The pharmaceutical compositions according to claim 1, wherein the NK_1 receptor antagonist is (S)-N-[2-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-2-[4-(2-hydroxy-1-hydroxymethyl-ethylamino)-piperidin-1-yl]-N-methyl-2-phenylacetamide or an acid addition salt thereof.

7. (Previously Presented) The pharmaceutical composition according to claim 1, wherein the weight ratio of the anticholinergic to the NK_1 receptor antagonist is in the range from 1:100 to 100:1.

8. (Previously Presented) The pharmaceutical composition according to claim 1, wherein a single administration corresponds to a dosage of the combination of the anticholinergic and the NK_1 receptor antagonist of 0.01 to 10,000 μg.

9. (Withdrawn) The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is in the form of a formulation suitable for inhalation.

10. (Withdrawn) The pharmaceutical composition according to claim 9, wherein the pharmaceutical composition is a formulation selected from among inhalable powders, propellant-containing metering aerosols and propellant-free inhalable solutions or suspensions.

11. (Withdrawn) The pharmaceutical composition according to claim 10, wherein the pharmaceutical composition is an inhalable powder which contains the anticholinergic and the NK_1 receptor antagonist in admixture with suitable physiologically acceptable excipients selected from the monosaccharides, disaccharides, oligo- and polysaccharides, polyalcohols, salts, or mixtures of these excipients.

12. (Withdrawn) The inhalable powder according to claim 11, wherein the excipient has a maximum average particle size of up to 250 μm.

13. **(Withdrawn)** A capsule containing an inhalable powder according to claim 11 or 12.

14. **(Withdrawn)** The pharmaceutical composition according to claim 10, wherein the pharmaceutical composition is an inhalable powder consisting essentially of the anticholinergic and the NK_1 receptor antagonist.

15. **(Withdrawn)** The pharmaceutical composition according to claim 10, wherein the pharmaceutical composition is a propellant-containing inhalable aerosol comprising the anticholinergic and the NK_1 receptor antagonist in dissolved or dispersed form.

16. **(Withdrawn)** The propellant-containing inhalable aerosol according to claim 15, wherein the propellant gas is n-propane, n-butane or isobutane, or chlorinated and/or fluorinated derivatives of methane, ethane, propane, butane, cyclopropane, or cyclobutane.

17. **(Withdrawn)** The propellant-containing inhalable aerosol according to claim 16, wherein the propellant gas is TG11, TG12, TG134a, TG227 or a mixture thereof.

18. **(Withdrawn)** The propellant-containing inhalable aerosol according to claim 15, further comprising one or more other ingredients selected from the group consisting of cosolvents, stabilizers, surfactants, antioxidants, lubricants and means for adjusting the pH.

19. **(Withdrawn)** The propellant-containing inhalable aerosol according to claim 15, wherein the inhalable aerosol contains up to 5 wt.-% of the anticholinergic and/or the NK_1 receptor antagonist.

20. **(Withdrawn)** The pharmaceutical composition according to claim 10, wherein the pharmaceutical composition is a propellant-free inhalable solution or suspension which contains water, ethanol or a mixture of water and ethanol as solvent.

21. **(Withdrawn)** The inhalable solution or suspension according to claim 20, wherein the pH is 2-7.

22. **(Withdrawn)** The inhalable solution or suspension according to claim 21, wherein the pH is adjusted by means of an acid selected from among hydrochloric acid, hydrobromic acid, nitric acid, sulphuric acid, ascorbic acid, citric acid, malic acid, tartaric acid, maleic acid, succinic acid, fumaric acid, acetic acid, formic acid and propionic acid or a mixture thereof.

23. **(Withdrawn)** The inhalable solution or suspension according to claim 20, further comprising other co-solvents and/or excipients.

24. **(Withdrawn)** The inhalable solution or suspension according to claim 23, wherein the co-solvents are isopropyl alcohol, propyleneglycol, polyethyleneglycol, polypropyleneglycol, glycolether, glycerol, polyoxyethylene alcohols or polyoxyethylene fatty acid esters.

25. **(Withdrawn)** The inhalable solution or suspension according to claim 23, wherein the excipients are surfactants, stabilizers, complexing agents, antioxidants and/or preservatives, flavorings, pharmacologically acceptable salts and/or vitamins.

26. **(Withdrawn)** The inhalable solution or suspension according to claim 25, wherein the complexing agent is editic acid or a salt of editic acid.

27. **(Withdrawn)** The inhalable solution or suspension according to claim 25, wherein the antioxidants are ascorbic acid, vitamin A, vitamin E, or tocopherols.

28. **(Withdrawn)** The inhalable solution or suspension according to claim 25, wherein the preservatives are cetyl pyridinium chloride, benzalkonium chloride, benzoic acid, or benzoates.

29. **(Withdrawn)** The inhalable solution or suspension according to claim 23, consisting essentially of the anticholinergic, the NK_1 receptor antagonist, the solvent, benzalkonium chloride, and sodium edetate.

30. (Withdrawn) The inhalable solution or suspension according to claim 23, consisting essentially of the anticholinergic, the NK_1 receptor antagonist, the solvent, and benzalkonium chloride.

31. (Withdrawn) The inhalable solution or suspension according to claim 20, wherein the inhalable solution or suspension is a concentrate or a sterile ready-to-use inhalable solution or suspension.

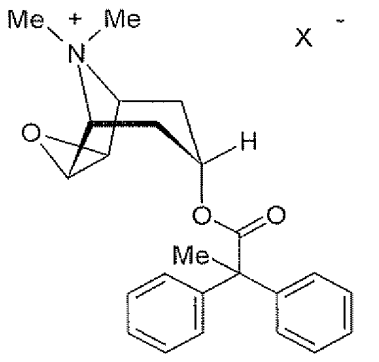
32. – 33. (Canceled)

34. (Withdrawn) The propellant-containing inhalable aerosol according to claim 17, wherein the propellant gas is TG134a, TG227 or a mixture thereof.

35. (Previously presented) A method of treatment of chronic obstructive pulmonary disease, comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical composition according to claim 1.

36. (Canceled)

37. (Previously presented) A method of treatment of chronic obstructive pulmonary disease, comprising administering simultaneously or sequentially to a mammal in need of such a treatment a therapeutically effective amount of a first pharmaceutical formulation comprising one or more anticholinergics of formula 1



wherein:

X^- is an anion with a single negative charge, or an enantiomer, mixture of the enantiomers, racemate, solvate, or hydrate thereof; and

a second pharmaceutical formulation comprising one or more NK_1 receptor antagonists or an enantiomer, mixture of the enantiomers, racemate, solvate, or hydrate thereof.

REMARKS

The Amendments

Claim 4 is amended to remove the "neuornorm" term and thus address the 35 U.S.C. §112, second paragraph, rejection. It is submitted that the above amendment would put the application in condition for allowance or materially reduce or simplify the issues for appeal. The amendment does not raise new issues or present new matter and does not present additional claims. The amendment has been made to render moot the 35 U.S.C. §112, second paragraph, rejection made in the Final action. Thus, it was not earlier presented. Accordingly, it is submitted that the requested amendment should be entered.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection under 35 U.S.C. §112, second paragraph

The rejection of claim 4 under 35 U.S.C. §112, second paragraph, is believed to be rendered moot by the amendment to claim 4.

The Rejection under 35 U.S.C. §103

The rejection of claims 1-8, 35 and 37 under 35 U.S.C. §103, as being obvious over Meissner (U.S. Patent No. 6,706,726) in view of Podolsky (US Pub. No. 2003/185838), is respectfully traversed.

Meissner discloses compounds of its formula I as anticholinergics, particularly for treating asthma or COPD (chronic obstructive pulmonary disease). Meissner does not

provide any suggestion of a composition of such compounds together with an NK_1 receptor antagonist.

Podolsky teaches that specific trefoil peptide compounds may be used to treat lesions of the respiratory epithelium. Use of certain trefoil peptide compounds is the main characterizing feature of Podolsky. Podolsky discloses that the lesions being treated can result from a wide variety of causes (see, e.g., page 1, paras. 0004 and 0010). It further discloses that these specific trefoil peptides may be used in combination with second therapeutic agents. Podolsky discloses a large variety of general second therapeutic agents which could possibly be used, i.e., anti-inflammatory agents, non-steroidal anti-inflammatory agents, antimicrobial agents, antihistamines, cholinergic receptor antagonists, neurokinin receptor antagonists, leukotriene receptor antagonists, decongestants, phosphodiesterase inhibitors and beta-adrenergic antagonists (see, e.g., page 1, para. 0012).

Applicants respectfully submit that one of ordinary skill in the art would not have been motivated by the reference teachings or have any other reason to combine one of the second therapeutic agents of Podolsky into the Meissner compositions or methods. Meissner is directed to methods and medicaments for treating COPD, whereas Podolsky is directed to methods and medicaments for treating lesions of the respiratory epithelium. Such lesions are not necessarily connected with COPD but are a symptom which can arise as a consequence of many of a variety of circumstances or diseases, for instance, from such varied sources as surgical intervention or intubation or by inhaling smoke, etc. (see, e.g., page 3, para. 0032, of Podolsky). One of ordinary skill in the art is not taught by Podolsky that any of its trefoil peptides or second therapeutic agents are effective to treat COPD but merely a symptom which might arise from it or from any of a number of other varied sources. COPD is only in certain situations connected with lesions of the respiratory epithelium, i.e., lesions of the

epithelium are not a general sympton in COPD. Further, lesions of the respiratory epithelium can also be caused by many different diseases and circumstances other than COPD.

For the above reasons, applicants respectfully urge that the instant facts are not in line with the citation in the Office action to In re Kerkhoven. Podolsky does not suggest the use of their second therapeutic agents to treat COPD. Thus, there is no motivation or other reason to combine any one of the second therapeutic agents of Podolsky, e.g., an NK receptor antagonist, with the anticholinergics of Meissner to treat COPD. In Kerkhoven, there was a reason to combine the two components because both were taught for the same specific use. Such is not the case here.

Further applicants urge that the In re Burckel decision cited in the Office action (and also KSR International Co. v. Teleflex Inc., 550 U.S. _, 82 USPQ2d 1385 (2007)) are not applicable to the instant facts. Applicants recognize that the reason for combining reference teachings need not be expressly stated in the cited references. Applicants' argument is that no reason – whether explicit, implicit or from application of common sense (see KSR) – for making the combination alleged in the Office action finds sufficient support on record. The apparent reason for combining the reference teachings is that both teach compounds for treating COPD. As discussed above, however, this reason is not supported by the facts. Podolsky does not teach that either its trefoil peptides or second therapeutic agents are should be used to treat COPD.

Even if one considered that Podolsky teaches treatment of COPD directly – which it clearly does not – one would not additionally conclude that the second therapeutic agents it teaches, e.g., NK receptor antagonists, would also be effective for treating COPD without the trefoil peptides. Podolsky just teaches that the specific trefoil peptides are effective to treat the lesions of the respiratory epithelium. Podolsky does not state whether its second

therapeutic agents are also useful for treating these lesions or have some other effect. One of ordinary skill in the art could not have a reasonable expectation that the second therapeutic agents, particularly a specific one, would be effective without being combined with the trefoil peptide.

Even if, contrary to all of the above reasons, one of ordinary skill in the art did have a reason to combine a second therapeutic agent of Podolsky into the Meissner compositions/methods, the claimed invention would still not be suggested. Podolsky teaches "neurokinin receptor antagonists" as only one broad category among a wide variety of possible second therapeutic agents. Given the broad teaching, one of ordinary skill in the art would not have been fairly directed to select this specific category of agent to combine with Meissner, particularly in view of the other distinctions discussed above. Further, Podolsky's teaching of "neurokinin receptor antagonists" does not point one of ordinary skill in the art to the specifically claimed invention, even if this category was selected. Podolsky does not teach, specifically, NK_1 antagonists (i.e., neurokinin receptor type 1 antagonists). There are at least three known neurokinin receptors types and nothing in the art points one of ordinary skill in the art to specifically select the NK_1 antagonists.

Further, both Meissner and Podolsky are silent as to the combined effect of an anticholinergic and NK_1 receptor antagonist. There is no suggestion that these compounds would be compatible or that their combination would be reasonably expected to succeed for treating a respiratory disease, particularly COPD, or for any other reason.

For all of the above reasons, it is urged that the combined teachings of the prior art fail to render the claimed invention obvious to one of ordinary skill in the art and the rejection under 35 U.S.C. §103 should be withdrawn.

It is submitted that the application is in condition for allowance. But the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

No fee, other than the One-Month Extension of Time being paid herewith, is believed to be due with this Reply. However, the Commissioner is hereby authorized to charge any additional fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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JAS/sb